

**WHAT WE CLAIM IS :**

1. Pharmaceutical combination comprising at least:
  - A first compound selected among the group consisting acetylsalicylic acid, salicylic acid, and pharmaceutical derivatives thereof, and
  - A second compound selected from the group consisting of lipidic betaines, betaines lipids, betaine of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with  $n$  an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof with the provision that said second compound is different from the first compound,in which said combination comprises less than 100 mg of said first compound expressed as acetylsalicylic acid, and  
in which the amount of second compound is at least 3 times the amount, calculated as acetylsalicylic acid weight, of said first compound.
2. The combination of claim 1, which comprises an amount of said first compound, calculated as acetylsalicylic acid, of less than 85 mg, advantageously of less than 75 mg, preferably of less than 60 mg.
3. The combination of claim 1, which comprises an amount of acetylsalicylic acid or pharmaceutical derivative thereof corresponding to 3 to 80 mg, advantageously from 5 to 75 mg, preferably from 10 to 75 mg calculated as acetylsalicylic acid.
4. The combination of claim 1, in which the amount of second compound is at least comprised between 3 and 100 times the amount calculated as acetylsalicylic acid weight of said first compound, advantageously comprised between 5 and 25 times the amount calculated as acetylsalicylic acid weight of said first compound.

5. The combination of claim 1 as an unitary dose, in which the amount of second compound is 60 times the amount, calculated as acetylsalicylic acid weight, of said first compound.
- 5 6. The combination of claim 1, which is prepared at least from a mixture in which at least 50% by weight of the first compound and at least 50% of the second compound are in soluble form.
7. The combination of claim 1, which is prepared at least from a mixture in  
10 which at least 90% by weight of the first compound and at least 90% of the second compound are in soluble form.
8. The combination of claim 1, which is prepared at least from a mixture in which the first compound and the second compound are substantially  
15 completely in soluble form.
9. The combination of claim 1, which the second compound is at least in a controlled release form.
- 20 10. The combination of claim 1, which the first compound is at least partly in an immediate release form.
11. The combination of claim 1, which comprises dry particles, especially micro particles, prepared by drying a mixture in which the first compound and  
25 the second compound are partly in a soluble form.
12. The combination of claim 1, in which the first compound and the second compound are combined in the form selected from the group consisting of a matrix, a gel, an hydrogel, a wax and a porous carrier, a bilayered tablet and  
30 combination thereof.

13. The combination of claim 1, which further comprises at least one compound reacting in presence of water so as to prepare substantially immediately a solution or suspension of first compound and second compound.

5 14. The combination of claim 1 in which the second compound comprise at least glycine betaine monohydrate.

15. The combination of claim 1 in which the second compound comprise at least glycine betaine anhydrous.

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16. Pharmaceutical unit dosage form comprising at least a pharmaceutical combination containing at least:

A first compound selected among the group consisting acetylsalicylic acid,  
15 salicylic acid, and pharmaceutical derivatives thereof, and

A second compound selected from the group consisting of lipidic betaines, betaines lipid, betaines of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with  $n$  an integer from 1 to 5, or a pharmaceutically acceptable salts thereof, esters thereof,  
20 precursors thereof, and mixtures thereof, with the provision that said second compound is different from the first compound, in which the combination is prepared from a mixture in which the first compound and the second compound are partly in a soluble form.

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17. The pharmaceutical form according to claim 16, which comprises less than 500 mg, advantageously less than 300 mg, preferably less than 100 mg of said first compound expressed as acetylsalicylic acid.

18. The pharmaceutical form according to claim 16, which the amount of second compound is at least 3 times the amount by weight of said first compound expressed as acetylsalicylic acid.

5 19. The pharmaceutical form of claim 16, in which the combination is prepared from a mixture in which at least 50% by weight of the first compound and at least 50% of the second compound are in soluble form.

20. The pharmaceutical form of claim 16, in which the combination is  
10 prepared from a mixture in which at least 90% by weight of the first compound and at least 90% of the second compound are in soluble form.

21. The pharmaceutical form of claim 16, in which the combination is prepared from a mixture in which the first compound and the second  
15 compound are substantially completely in soluble form.

22. The pharmaceutical form of claim 16, in which the combination is in the form of dry particles, especially micro particles, prepared by drying a mixture in which the first compound and the second compound are partly in a soluble  
20 form.

23. The pharmaceutical form of claim 16, in which the combination is in the form selected from the group consisting of a matrix, a gel, an hydrogel, a wax and a porous carrier and combinations thereof.

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24. The pharmaceutical form of claim 16, which is at least a controlled release formulation for the second compound.

25. The pharmaceutical form of claim 16, which is at least an immediate  
30 release formulation for the first compound.

26. The pharmaceutical form of claim 16, which further comprises at least one compound reacting in presence of water so as to prepare substantially immediately a solution or suspension of first compound and second compound.
- 5 27. The pharmaceutical form of claim 16, in which second compound is glycine betaine or a pharmaceutical salt thereof.
28. A kit for a daily administration, said kit comprising at least:
- 10 - An first oral formulation comprising a first compound selected among the group consisting acetylsalicylic acid, salicylic acid, and pharmaceutical derivatives thereof, and
- A second oral formulation comprising a second compound selected from the group consisting of lipidic betaines, betaines lipids, betaines of formula
- 15  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with n an integer from 1 to 5, or a pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof, with the provision that said second compound is different from the first compound
- in which the first oral formulation comprises less than 100 mg of said first
- 20 compound expressed as acetylsalicylic acid, and
- in which the amount of second compound in the second oral formulation is at least three times the amount, calculated as acetylsalicylic acid, of said first compound.
- 25 29. The kit of claim 28, in which the first oral formulation comprises an amount of said first compound, calculated as acetylsalicylic acid, of less than 85 mg, advantageously of less than 75 mg, preferably of less than 60 mg.
30. The kit of claim 28, in which the first oral formulation comprises an
- 30 amount of acetylsalicylic acid or pharmaceutical derivative thereof

corresponding to 3 to 80 mg, advantageously from 5 to 75 mg, preferably from 10 to 75 mg calculated as acetylsalicylic acid.

31. The kit of claim 28, in which the second oral formulation comprises an amount of second compound corresponding to at least 5 times the amount by weight, calculated as acetylsalicylic acid, of said first compound.

32. The kit of claim 28, in which the second oral formulation comprises an amount of second compound corresponding to 10 times to 100 times by weight, calculated as acetylsalicylic acid, of said first compound.

33. The kit of claim 28, in which the first oral formulation comprises an amount of a second compound selected from the group consisting of betaines of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with  $n$  an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof, with the provision that said second compound is different from the first compound.

34. The kit of claim 28, in which the first oral formulation is prepared at least from a mixture in which at least 50% by weight of the first compound and at least 50% of the second compound are in soluble form.

35. The kit of claim 28, in which the first oral formulation is prepared at least from a mixture in which at least 90% by weight of the first compound and at least 90% of the second compound are in soluble form.

36. The kit of claim 28, in which the first oral formulation is prepared at least from a mixture in which the first compound and the second compound are substantially completely in soluble form.

37. The kit of claim 28, in which the second oral compound is at least in a controlled release form.

38. The kit of claim 28, in which the first oral compound is at least in a  
5 immediate release form.

39. The kit of claim 28, in which the second oral formulation is at least glycine betaine and its pharmaceutically acceptable salts.

10 40. The use of

- a first compound selected among the group consisting acetylsalicylic acid, salicylic acid, pharmaceutical derivatives thereof, and

- a second compound selected from the group consisting of lipidic  
15 betaines, betaines lipids, betaines of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with n an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof, with the provision that said second compound is different from the first compound,

for the preparation of a pharmaceutical combination according to anyone of  
20 the claims 1 to 15 or a pharmaceutical dosage form according to anyone of the claims 16 to 27 or a kit according to any one of the claims 28 to 39, for treating or preventing blood flow disturbances.

41. The use of

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- a first compound selected among the group consisting acetylsalicylic acid, salicylic acid, pharmaceutical derivatives thereof, and

- a second compound selected from the group consisting of lipidic  
30 betaines, betaines lipids, betaines of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with n an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof,

precursors thereof, and mixtures thereof, with the provision that said second compound is different from the first compound,

for the preparation of a pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical dosage form according to anyone of the  
5 claims 16 to 27 or a kit according to any one of the claims 28 to 39, for treating or preventing cancer.

#### 42. The use of

- 10 - a first compound selected among the group consisting acetylsalicylic acid, salicylic acid, pharmaceutical derivatives thereof, and  
- a second compound selected from the group consisting of lipidic betaines, betaines lipids, betaines of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with n an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof,  
15 precursors thereof, and mixtures thereof, with the provision that said second compound is different from the first compound,

for the preparation of a pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical dosage form according to anyone of the claims 16 to 27 or a kit according to any one of the claims 28 to 39, for treating  
20 or preventing diabetes.

#### 43. The use of

- a first compound selected among the group consisting acetylsalicylic  
25 acid, salicylic acid, pharmaceutical derivatives thereof, and  
- a second compound selected from the group consisting of lipidic betaines, betaines lipids, betaines of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with n an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof, with the provision that said second  
30 compound is different from the first compound,



for the preparation of a pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical dosage form according to anyone of the claims 16 to 27 or a kit according to any one of the claims 28 to 39, for treating or preventing gut.

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44. The use of

- a first compound selected among the group consisting acetylsalicylic acid, salicylic acid, pharmaceutical derivatives thereof, and

10 - a second compound selected from the group consisting of lipidic betaines, betaines lipids, betaines of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with n an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof, with the provision that said second compound is different from the first compound,

15 for the preparation of a pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical dosage form according to anyone of the claims 16 to 27 or a kit according to any one of the claims 28 to 39, for treating or preventing inflammation.

20 45. Process of treatment of a patient in need for treating, preventing, reducing thrombosis troubles for a patient, by administering to said patient a pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical unit dose according to anyone of the claims 16 to 27, in which advantageously before and/or during and/or after said administration, a  
25 therapeutic effective amount of glycine betaine is further administered to said patient.

46. Process of treatment of a patient in need for treating, preventing, reducing inflammation troubles in a patient, by administering to said patient a  
30 pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical unit dose according to anyone of the claims 16 to 27, in which

advantageously before and/or during and/or after said administration, a therapeutic effective amount of glycine betaine is further administered to said patient.

5 47. Process of treatment of a patient in need for treating, preventing, reducing inflammation troubles in a patient, by administering to said patient a pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical unit dose according to anyone of the claims 16 to 27, in which advantageously before and/or during and/or after said administration, a  
10 therapeutic effective amount of glycine betaine is further administered to said patient.

48. Process of treatment of a patient in need for treating, preventing, reducing  
15 inflammation troubles in a patient, by administering to said patient a pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical unit dose according to anyone of the claims 16 to 27, in which advantageously before and/or during and/or after said administration, a therapeutic effective amount of glycine betaine is further administered to said  
20 patient.

49. Process of treatment of a patient in need for treating, preventing, reducing gut troubles in a patient, by administering to said patient a pharmaceutical combination according to anyone of the claims 1 to 15 or a pharmaceutical unit  
25 dose according to anyone of the claims 16 to 27, in which advantageously before and/or during and/or after said administration, a therapeutic effective amount of glycine betaine is further administered to said patient.

30 50. A pharmaceutical composition comprising a betaine and aspirin in a formulation wherein the betaine and aspirin are formulated together in a

bilayered tablet, the aspirin being present in a first layer, and the betaine being present in a second layer in an amount at least three times the amount of aspirin.

- 5 51. The pharmaceutical composition as defined in claim 50, wherein the layer containing the betaine also includes one or more buffering agents.
52. The pharmaceutical composition as defined in claim 50, wherein the tablet includes a core and a coating layer surrounding said core and wherein  
10 one of the betaine and aspirin is present in the core and the other is present in a coating layer surrounding the core.
53. The pharmaceutical composition as defined in claim 50, wherein the tablet includes a core and a coating layer surrounding said core and wherein a  
15 mixture of the betaine and aspirin is present in the core and one of the betaine and aspirin is present in the coating layer surrounding the core.
54. The pharmaceutical composition as defined in claim 52, wherein the aspirin is present in the core and the betaine is present in the coating layer.  
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55. The pharmaceutical composition as defined in anyone of the claims 52 to 54, wherein the aspirin is present in the core and the betaine present in the coating layer is in a controlled release form.
- 25 56. The pharmaceutical composition as defined in anyone of the claims 52 to 54, wherein the betaine is present in the core in a controlled release form and the aspirin is present in the coating layer.
57. The pharmaceutical composition as defined in claim 53 wherein the  
30 coating layer also includes one or more buffering agents.

58. The pharmaceutical composition as defined in claim 54 wherein the coating layer also includes one or more buffering agents and one or more protecting films.

5 59. The pharmaceutical composition as defined in claim 50 wherein the betaine is selected from the group consisting of betaines of formula  $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$  with n an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof.

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60. The pharmaceutical composition as defined in claim 50 further including an outer protective coating or finishing layer surrounding said tablet.

15 61. The pharmaceutical composition as defined in claim 50 wherein the aspirin is in the form of enteric coated aspirin granules.

62. The pharmaceutical composition as defined in claim 1 in the form of a bilayered tablet which comprises a first layer comprising aspirin granules and one or more excipients, and a second layer comprising a betaine and one or  
20 more buffering compounds and one or more excipients.

63. The pharmaceutical composition as defined in claim 60, wherein the first layer comprises aspirin granules, one or more bulking agents and optionally a lubricant, and the second layer comprises a betaine, optionally a wet  
25 granulating agent, one or more buffering compounds selected from the group consisting of calcium carbonate, magnesium oxide, magnesium carbonate and mixtures thereof, and optionally magnesium stearate.

64. The pharmaceutical compositions as defined in anyone of the claims 50 to  
30 63 further including an outer protective coating surrounding said bilayered tablet.

65. The pharmaceutical compositions as defined in anyone of the claims 50 to 63 further including an antithrombotic agent.
- 5 66. The pharmaceutical composition as defined in anyone of the claims 50 to 63 further including an anti cancerous agent.
67. The pharmaceutical composition as defined in anyone of the claims 50 to 63 further including an anti inflammatory agent.
- 10 68. The pharmaceutical composition as defined in anyone of the claims 50 to 63 further including an antibiotic agent.
69. The pharmaceutical composition as defined in anyone of the claims 50 to 15 63 further including an anti diabetic agent.
70. The pharmaceutical composition as defined in anyone of the claims 50 to 63 further including an antioxidant agent
- 20 71. A method for preventing or inhibiting or treating atherosclerosis or reducing risk of or treating a cardiovascular event or disease, coronary artery disease or cerebro-vascular disease, which comprises administering to a patient in need of treatment a therapeutically effective amount of a pharmaceutical composition according to claim 50.
- 25 72. The method as defined in claim 71, wherein the betaine employed is anhydrous and/or monohydrate salt, and/or lipidic betaine and/or betaine lipids.
73. A pharmaceutical composition comprising betaine and aspirin in a 30 formulation to reduce aspirin side effects wherein the betaine and aspirin are

formulated together in a bilayered tablet, the aspirin being present in a first layer, and the betaine being present in a second layer.

- 5 74. A pharmaceutical composition comprising betaine and aspirin in a formulation to increase aspirin therapeutic effects wherein the betaine and aspirin are formulated together in a bilayered tablet, the aspirin being present in a first layer, and the betaine being present in a second layer.

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